MAY 3 1 2002

4.0 SUMMARY OF SAFETY AND EFFECTIVENESS

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Date of Summary: May 22, 2002
Device Trade Name: AxSYM® Intact PTH
Regulation Cite: 21CFR862.1545
Classification Name: Parathyroid Hormone
Analyte Code and Name: (CEW) Parathyroid Hormone Test System
Regulatory Class: II

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92 to provide sufficient detail to understand the basis for a determination of substantial equivalence.

The assigned 510(k) number is: K020945

4.1 Test Description:

4.1.1 Parathyroid hormone (PTH, parathyrin) is synthesized as a pre-pro hormone by the chief cells of the parathyroid glands [1,2]. In normal physiology, PTH levels increase in response to decreased serum calcium and decrease in response to increased serum calcium resulting in a close inverse relationship between PTH and calcium concentrations [1,6]. Abnormal PTH levels can thus be detected by examining this interrelationship. Concurrent increases in PTH and calcium occur in the various forms of hyperparathyroidism, including multiple endocrine neoplasia (MEN) types I and II, parathyroid tumors, and idiopathic hyperparathyroidism [6,7]. Concurrent declines in calcium and PTH occur in the various forms of primary hypoparathyroidism and in disorders affecting PTH secretion, such as hypo- or hyper-magnesemia [8]. Abnormally low calcium levels in the presence of extremely elevated PTH levels can occur in a group of genetic disorders called pseudohypoparathyroidism [9]. Abnormally high calcium levels in the presence of low or normal PTH levels are characteristic of malignancy-associated hypercalcemia secondary to PTH-related peptide (PTHrP) production [10]. Abnormal concentrations and/or actions of PTH with essentially normal serum calcium levels may also occur, e.g. in renal osteodystrophy [11].

NOTE: The bibliography notations used make reference to the Bibliography Section at the end of the AxSYM I PTH Package Insert.

4.1.2 Immunoassays for I-PTH and its two major metabolic fragments have been developed. Clinical investigations indicate that the diagnostic sensitivities of the N-terminal and C-terminal assays are limited, possibly due in part to variable concentrations of minor fragments and the performance characteristics of the assays [1,4]. Selective measurement of mainly I PTH has theoretical advantages since it may be more reflective of biologically active PTH production and action.

4.1.3 The AxSYM® I PTH assay uses paired monoclonal and polyclonal antibodies, each reactive with epitopes in the N-terminal portion of intact human PTH (1-84). The polyclonal antibody is biotin labeled. I PTH in the sample serves to bridge the two antibodies.

4.2 Principle Of The Test:

4.2.1 AxSYM® I PTH is based on the Microparticle Enzyme Immunoassay (MEIA) technology.

The AxSYM® I PTH reagents and sample are pipetted in the following sequence:

4.2.2 SAMPLING

- Sample and all AxSYM® I PTH Reagents required for one test are pipetted by the sampling probe into various wells of a Reaction Vessel (RV).

  The RV is immediately transferred into the Processing enter. Further pipetting is done in the Processing Center by the Processing Probe.

4.2.3 PROCESSING

- An aliquot of the reaction mixture containing the antibody-antigen complex bound to the microparticles is transferred to the matrix cell. The microparticles bind irreversibly to the glass fiber matrix..
- The matrix cell is washed with the TRIS Wash Buffer.
- The Anti-PTH: Biotin Conjugate is dispensed onto the matrix cell and binds with the antibody-antigen complex.
- The matrix cell is washed to remove unbound materials.
- The Anti-Biotin: Alkaline Phosphatase Conjugate is then dispensed onto the matrix cell and binds with the biotinylated antibody-antigen complex.
- The matrix cell is washed to remove unbound materials.
- The substrate, 4-Methylumbelliferyl Phosphate, is added to the matrix cell and the fluorescent product is measured by the MEIA optical assembly.

4.3 Intended Use:

AxSYM® Intact PTH is a Microparticle Enzyme Immunoassay (MEIA) for the *in vitro* quantitative determination of intact human parathyroid hormone (I PTH) in human serum or plasma on the AxSYM® system. The AxSYM® I PTH assay is intended for use as an aid in the differential diagnosis of hypercalcemia and hypocalcemia.

4.4 Substantial Equivalence:

4.4.1 The AxSYM® Intact PTH assay is substantially equivalent to another device marketed in the United States. We claim equivalence to the DSL-8000 ACTIVE™ Intact PTH IRMA (K896294).

4.4.2 To demonstrate substantial equivalence between the two assays, serum and plasma samples were assayed using both methods. Method correlation between the AxSYM® I PTH and the predicate device was examined using 120 samples. The resulting regression equation was determined to be:

[AxSYM® I PTH] = 0.99 [DSL ACTIVE™ I PTH IRMA] + 10.0
$r = 0.97$
$p < 0.0001$

The results of least squares regression analysis indicated very high correlation between the two methods ($r = 0.97$). The 95% confidence interval about the slope is [95% CI (0.95, 1.05)]. This correlation between the two methods is highly significant ($p<0.0001$). The 95% CI about the intercept is [95% CI (-11.72, 31.82)]. The intercept is not statistically significant ($p<0.35$).

Specimen values ranged from 4 - 1961 pg/mL with the AxSYM® I PTH and 6 – 1836 pg/mL with the predicate device, DSL ACTIVE™ Intact PTH IRMA.

Similarities: The following table compares the similarities between the AxSYM® I PTH assay with the predicate device:

Feature	AxSYM® I PTH	Predicate Device (K896294)
Assay Principle	Sandwich Assay	Sandwich Assay
Intended Use	for the *in vitro* quantitative determination of intact human parathyroid hormone (I PTH) in human serum or plasma on the AxSYM® system	for the quantitative measurement of Intact PTH (I-PTH) in serum or plasma.
Indication for Use	an aid in the differential diagnosis of hypercalcemia and hypocalcemia	None stated in package insert
Sample type	Human serum or plasma	Human serum or plasma
Sample required	185 µL	200 µL
Dynamic Range	0 - 2000 pg/mL	0 - 2000 pg/mL
Expected Values	8 – 57.8 pg/mL	9 - 55 pg/mL
Traceability	Traceable to DSL I PTH IRMA	Traceable to Nichols I PTH Assay

Differences: The following table compares the differences between the AxSYM I PTH assay and the predicate device:

Feature	AxSYM® I PTH	Predicate Device (K896294)
Assay Technology	Microparticle Enzyme Immunoassay (MEIA) employing the "sandwich" principle	Immunoradiometric Assay (IRMA) employing the "sandwich" principle
Instrument	AxSYM Immunoassay Analyzer	Gamma Counter

Performance Characteristics: The following table compares the assay performance characteristics between the AxSYM® I PTH and the predicate device:

Characteristics	AxSYM® Intact PTH	Predicate Device (K896294)
Precision (Within Run)	Level I (35.3 pg/mL): 5.9 % CV	Level I (13.0 pg/mL): 3.1 % CV
	Level II (202.9 pg/mL): 6.2 % CV	Level II (23.0 pg/mL): 3.5 % CV
	Level III (649.7 pg/mL): 6.5 % CV	Level III (476 pg/mL): 1.9 % CV
Precision (Inter)	Level I (35.3 pg/mL): 9.4 % CV	Level I (13.0 pg/mL): 3.1 % CV
	Level II (202.9 pg/mL): 8.1 % CV	Level II (23.0 pg/mL): 5.2 % CV
	Level III (649.7 pg/mL): 8.8 % CV	Level III (472.0 pg/mL): 2.6 % CV
Linearity (Mean ± SD)	93.8 ± 8.9 %	94.2 ± 10.5 %
Recovery (Mean ± SD)	95.3 ± 8.9 %	97.7 ± 5.2 %
Analytical Sensitivity	≤ 2.0 pg/mL I PTH	6.0 pg/mL I PTH
Specificity	No detection of human PTH fragments 53-84, 44-68 and 39-84	No detection of human PTH fragments 53-84, 44-68 and 39-84
Interference	Bilirubin (20 mg/dL): < 10 %	ND
	Triglycerides (1500 mg/dL): < 10 %	ND
	Total Protein (3 mg/dL): < 10 %	ND
	Hemoglobin (1000 mg/dL): < 10 %	ND
	Red Blood Cells (0.2 % v/v): < 10 %	ND
Limitations	No high dose effect up to 100K pg/mL	No high dose effect up to 300K pg/mL
On-board Stability	14 days @ 31^0C	N/A

ND = Not Determined N/A = Not Applicable

4.5 Safety & Effectiveness:

4.5.1 As explained in Section 4.1 of this submission, the I PTH levels are used in conjunction with calcium levels as a clinical diagnostic tool to support the diagnosis of a disorder, as explained in the **Summary and Explanation of the Test** in the beginning of the AxSYM® I PTH Package Insert in Section 6.0. The I PTH assay is not used as a stand-alone test. Clinical interpretation requires simultaneous measurement of serum calcium levels. The levels of I PTH and calcium are repeated over a period of time for a diagnosis and during any type of treatment for effectiveness.

4.5.2 The safety of use for both I PTH assays is substantially equivalent, but the AxSYM® I PTH assay has less risk associated with it due to the absence of radioactive materials.

4.5.3 Therefore, we conclude the safety and effectiveness of both assays are substantially equivalent and favor the AxSYM® I PTH assay.

4.6 Substantial Equivalence Conclusion

We conclude that the data and information supplied in this summary provide enough detail and support for our claim of substantial equivalence between the AxSYM® Intact PTH assay and the predicate device, DSL-8000 ACTIVE™ Intact PTH IRMA.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAY 31 2002

Mr. Carroll Potts, M.S.
Manager of Regulatory Affairs
Diagnostic Systems Laboratories, Inc.
445 Medical Center Blvd.
Webster, TX 77598

Re: k020945
Trade/Device Name: AxSYM® Intact PTH
Regulation Number: 21 CFR 862.1545; 21 CFR 862.1150; 21 CFR 862.1660
Regulation Name: Parathyroid hormone test system; Calibrator; Quality control material (assayed and unassayed)
Regulatory Class: Class II
Product Code: CEW; JIT; JIX
Dated: March 22, 2002
Received: March 25, 2002

Dear Mr. Potts:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory-Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

1.0 INDICATIONS FOR USE

510 (k) Number (if known): K020945

Device Name: AxSYM® Intact PTH

Indications for Use:

AxSYM® Intact PTH is a Microparticle Enzyme Immunoassay (MEIA) for the *in vitro* quantitative determination of intact human parathyroid hormone (I PTH) in human serum or plasma on the AxSYM® system. The AxSYM® I PTH assay is intended for use as an aid in the differential diagnosis of hypercalcemia and hypocalcemia.

Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K020945

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ **OR** **Over-The Counter Use** _____
(Per 21 CFR 801.109)